85. (New) A diagnostic kit comprising:

(a) at least one oligonucleotide that hybridizes under moderately stringent conditions to a polynucleotide sequence comprising a sequence selected from the group consisting of:

(i) SEQ ID NO:21, and

(ii) sequences having at least 90% identity to SEQ ID NO:21; and

(b) a reporter group for use in a polymerase chain reaction or hybridization assay.

REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the following remarks. Claims 65-78 have been cancelled and new claims 79-85 have been added for purposes of clarity and to place this application in better condition for allowance and/or appeal. It is urged that support for all the above amendments and new claims may be found throughout the specification as originally filed and that none of these amendments or new claims constitutes new matter. Specifically, support for hybridization assays can be found on page 46, line 31 – page 47, line 17 and support for reporter groups on page 20, line 22 – line 27. It should also be noted that the above amendments are made without prejudice to prosecution of any or all subject matter modified and/or removed by this amendment in a related divisional, continuation and/or continuation-in-part application.

Rejections under 35 USC 101 (Utility)

Claims 65-70 and 76-78 stand rejected under 35 USC §101 as allegedly lacking either an asserted utility or a well-established utility. The Examiner has further rejected claims 65-70 and 76-78 under 35 USC §112, first paragraph as allegedly lacking

an enabling description of how to use the claimed invention. These rejections are respectfully traversed.

As described in the specification from page 53 line 7 - line 10, Contig 18 (SEQ ID NO:21) shows homology to the known gene for L1-Cadherin and shows over-expression in approximately half of colon tumors and low level overexpression in 3/6 normal colon tissues tested. This sequence is not significantly expressed in any other normal tissues tested.

The Examiner contends that claimed SEQ ID NO:21 fails to have utility on the basis that some expression of this sequence was observed in normal colon tissue. The Examiner further asserts that the specification does not teach how such a putative polypeptide is associated with any cancer. Applicants respectfully traverse this rejection on the grounds that, although differential overexpression of a sequence in tumor tissue versus normal tissue of the same tissue type is certainly one basis upon which a sequence can have diagnostic utility, the skilled artisan would appreciate that this is not the only basis. For example, a colon-specific sequence can be used in the detection of metastatic colon cancer cells that have escaped the site of a primary colon tumor and entered the circulation. In this diagnostic scenario, detection of overexpression of a sequence comprising SEQ ID NO:21 in circulation as compared to non-colon normal tissue is all that is required for detection of metastatic colon cancer cells in the patient's serum.

Moreover, techniques for employing the inventive DNA molecules in the detection of colon cancer are well known in the art and include PCR based assays, hybridization assays, and the like, as described throughout the specification as originally filed, for example on page 46, line 25 – page 47, line 17. It is urged that it would be well within the abilities of one of skill in the art, on being provided with the instant specification, to use the claimed DNA molecules in a diagnostic context.

The Examiner further alleges that the specification does not teach a function for the polypeptide encoded by SEQ ID NO:21. Applicants urge that the function of the polypeptide encoded by SEQ ID NO:21 per se is irrelevant to the use of the polynucleotide of SEQ ID NO:21 in the diagnosis or monitoring of colon cancer. As stated above, the relevant function of the polynucleotide of SEQ ID NO:21 is its

overexpression in colon tissue. As stated in the specification, SEQ ID NO:21 is overexpressed in colon tissue and, as such, Applicants have described a unique identifying characteristic of this polynucleotide and, as discussed above, its well-established utility in the diagnosis and monitoring of colon cancer.

In light of the above remarks, Applicants submit that the rejections of claims 65-70 and 76-78 under 35 USC §101, as lacking a specific utility, and under 35 USC §112, first paragraph, as lacking an enabling description, have been overcome and respectfully request that the Examiner issue a Notice to that effect.

Rejections under 35 USC 112, first paragraph (enablement)

Claims 65-70 and 76-78 are rejected as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the claimed polynucleotide sequences.

The Examiner alleges that the claims are not enabled because the specification has not taught the degree of homology between SEQ ID NO:21 and L1-Cadherin and that the citation of sequence homology results in an unpredictable and therefore unreliable correspondence between the claimed biomolecule and the indicated similar biomolecule and therefore lacks enabling support.

Applicants respectfully traverse this rejection and request reconsideration and withdrawal of the rejection in light of the following remarks. The specification teaches on page 7, lines 17 and 18, and page 53, line 7 - line 10, that the polynucleotide sequence set forth in SEQ ID NO:21 shows homology to the known gene, L1-Cadherin. Applicants submit that it is well known in the art how to determine the level of identity of 2 (or more) sequences and that a skilled artisan would be able to determine, through routine experimentation, that SEQ ID NO:21 corresponds to L1-Cadherin. Moreover, the specification clearly teaches (on page 16, line 5 – line 26), a preferred method for determining the percent identity between 2 or more sequences. Thus, Applicants submit that the specification as filed satisfies the enablement requirement of 35 USC 112, first paragraph, and respectfully urge that the rejection may be properly withdrawn.

The Examiner further asserts that the specification does not provide guidance as to what the amount of DNA is indicative of the presence or absence of cancer. The Examiner makes a similar assertion with regard to determining the progression of cancer in a patient. Applicants respectfully disagree and direct the Examiner to page 14, lines 25-27, for example, where the specification clearly defines a "colon tumor protein" as

> "...a protein that is expressed in colon tumor cells at a level that is **at least two fold**, and preferably at least five fold, greater than the level of expression in a normal tissue..." (emphasis added)

Furthermore, the specification teaches on page 52, lines 10-11, that the isolated cDNAs (including SEQ ID NO:21) showed **two or more fold over-expression in the colon tumor probe group as compared to the normal tissue probe group** (emphasis added). Thus, Applicants submit that a skilled artisan would readily appreciate how much DNA is indicative of the presence or absence of cancer. Moreover, the specification clearly defines how to determine the progression of cancer in a patient on page 47, line 28 – page 48, line 5. Applicants submit that a skilled artisan would readily appreciate how to determine the presence or absence of cancer, and/or determine the progression of cancer in a patient in light of the guidance of the specification as filed, without undue experimentation. Therefore, Applicants submit that the specification, as filed, satisfies the enablement requirement of 35 USC 112, first paragraph and respectfully urge that the rejection may be properly withdrawn.

The Examiner further alleges in point 6 of the present Office Action that the specification does not enable the skilled artisan to make or use the invention commensurate in scope with the present claims. Thus, the Examiner alleges that Applicants are not entitled to open "comprising" language recited in the claims because the specification does not teach the full length cDNA sequence encompassed by SEQ ID NO:21 nor does the specification set forth any functional characteristics that are specific to the protein encoded by SEQ ID NO:21.

Applicants respectfully traverse this rejection and submit that the present disclosure more than adequately meets the enablement requirement of 35 USC § 112. All that is required of Applicants to comply with the enablement requirements of 35 USC § 112 is that the disclosure provide sufficient teaching to permit one skilled in the art to practice the full scope of the claimed invention without undue experimentation.

The presently claimed invention is directed to a polynucleotide (represented by SEQ ID NO:21) that is differentially expressed in tumor tissue versus normal tissues, and to the use of sequence comprising SEQ ID NO:21, for example, in the detection of cancer. As is noted above and as described in the attached Declaration of Dr. Susan Harlocker, SEQ ID NO: 21 is a fragment of the known polynucleotide sequence of L1 cadherin. Therefore, at the time the present application was filed, a skilled artisan could, through routine experimentation, have identified, in the publicly available databases, a full-length sequence comprising the polynucleotide of SEQ ID NO: 21. Thus, guided with the SEQ ID NO: 21 colon tumor expression data disclosed in the application coupled with the various methodologies for oligonucleotide detection either explicitly disclosed or otherwise incorporated by reference, Applicants respectfully submit that one of skill in the art could have practiced the presently claimed methodologies and kits for the detection of colon cancer without undue experimentation.

The skilled artisan would have recognized that SEQ ID NO:21 represents a portion of a discrete mRNA expressed in humans. The skilled artisan would also have recognized that the expression profiles of mRNAs consisting of SEQ ID NO:21 would be indistinguishable from the expression profiles of the corresponding full-length cDNA sequences, *i.e.*, sequences comprising SEQ ID NO:21. Moreover, the claimed methods and kits comprising oligonucleotides that hybridize to a polynucleotide that encodes a colon tumor protein comprising an amino acid sequence encoded by SEQ ID NO:21 for the detection of cancer, were thus clearly defined in terms of structure. The claimed invention was also defined, as discussed above, in terms of function in that SEQ ID NO:21 is overexpressed in colon cancer as compared to non-colon normal tissues. Therefore, considering the present disclosure in its entirety, it is submitted that the skilled

artisan would be enabled to make and use the claimed diagnostic methods employing polynucleotides comprising SEQ ID NO:21.

On the basis on these arguments, Applicants respectfully submit that the pending claims are fully enabled by the present specification as required by 35 USC §112, first paragraph, and respectfully request reconsideration and withdrawal of the Examiner's present basis for rejection.

Rejections under 35 USC 112, first paragraph (written description)

Claims 76-78 are rejected as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner alleges, as in the enablement rejection above, that Applicants are not entitled to open "comprising" language recited in the claims because the specification does not teach the full-length cDNA sequence which is encompassed by SEQ ID NO:21.

Applicants respectfully traverse this rejection. As noted above, and as described in the attached Declaration of Dr. Susan Harlocker, SEQ ID NO:21 is a fragment of the polynucleotide that encodes L1 cadherin the sequence of which polynucleotide was publicly available at the time Applicants filed the present application. Furthermore, the skilled artisan would also have recognized that the expression profiles of polynucleotides consisting of SEQ ID NO:21 would be identical with the expression profiles of polynucleotides comprising SEQ ID NO:21. Thus, Applicants submit that the specification need not explicitly set forth the full-length L1 cadherin polynucleotide sequence in order for one skilled in the art to recognize that Applicants were in possession of the presently claimed methods and kits for the detection and monitoring of colon cancer wherein the methods and kits comprise oligonucleotides that hybridize to polynucleotides comprising SEQ ID NO:21.

In view of the present arguments and attached Declaration of Dr. Susan Harlocker, it is urged that the pending claims fully satisfy the written description

requirements of 35 USC §112, first paragraph, and respectfully request that this basis for rejection be withdrawn.

Rejection under 35 USC 102

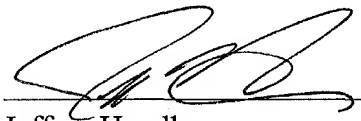
Claims 76 and 77 are rejected under 35 USC 102(b) as being anticipated by accession number Z67986.

Without acquiescing to the Examiner's rejection, claims 76 and 77 have been canceled. Thus, Applicants submit that this ground for rejection has been obviated and respectfully request its withdrawal.

Favorable reconsideration and allowance of the pending claims are respectfully requested. The Examiner is invited to contact the undersigned with any questions, concerns or suggestions pertaining to this communication.

Respectfully submitted,

Seed Intellectual Property Law Group PLLC



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Enclosures:

Declaration of Susan Harlocker, Ph.D.
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VERSION WITH MARKINGS TO SHOW CHANGES

In the claims:

Claims 79-85 have been added as follows:

79. (New) A method for determining the presence of colon cancer in a patient, comprising the steps of:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide that hybridizes under moderately stringent conditions to a polynucleotide sequence comprising a sequence selected from the group consisting of:

(iii) SEQ ID NO:21, and

(iv) sequences having at least 90% identity to SEQ ID NO:21;

(c) detecting in the sample an amount of oligonucleotide that hybridizes to the polynucleotide; and

(d) comparing the amount of oligonucleotide that hybridizes to the polynucleotide to a predetermined cut-off value, wherein an increase in the amount of oligonucleotide that hybridizes to the polynucleotide as compared to the predetermined cut-off value indicates the presence of cancer in the patient.

80. (New) The method according to claim 79 wherein the amount of oligonucleotide that hybridizes to the polynucleotide is determined using a polymerase chain reaction.

81. (New) The method according to claim 79 wherein the amount of oligonucleotide that hybridizes to the polynucleotide is determined using a hybridization assay.

82. (New) A method for monitoring the progression of colon cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

(b) contacting the biological sample with an oligonucleotide that hybridizes under moderately stringent conditions to a polynucleotide sequence comprising a sequence selected from the group consisting of:

(iii) SEQ ID NO:21, and

(iv) sequences having at least 90% identity to SEQ ID NO:21;

(f) detecting in the sample an amount of oligonucleotide that hybridizes to the polynucleotide;

(g) repeating steps (a)-(c) wherein the biological sample is obtained from the patient at a subsequent point in time; and

(h) comparing the amount of oligonucleotide detected in (d) to the amount detected in (c) wherein an increase in the amount of oligonucleotide in step (d) as compared to the amount of oligonucleotide in step (c) indicates progression of said colon cancer and wherein a decrease in the amount of oligonucleotide in step (d) as compared to the amount of oligonucleotide in step (c) indicates a remission of said colon cancer.

83. (New) The method according to claim 82 wherein the amount of oligonucleotide that hybridizes to the polynucleotide is determined using a polymerase chain reaction.

84. (New) The method according to claim 82 wherein the amount of oligonucleotide that hybridizes to the polynucleotide is determined using a hybridization assay.

85. (New) A diagnostic kit comprising:

(a) at least one oligonucleotide that hybridizes under moderately stringent conditions to a polynucleotide sequence comprising a sequence selected from the group consisting of:

(iii) SEQ ID NO:21, and

(iv) sequences having at least 90% identity to SEQ ID NO:21; and

(b) a reporter group for use in a polymerase chain reaction or hybridization assay.